

AMENDMENTS TO THE SPECIFICATION

Applicant respectfully requests that the Examiner make the following amendments to the Specification:

Replace the exiting title to read “Generating a Unique Sequence Database.”

AMENDMENTS TO THE CLAIMS

Applicant respectfully requests that the Examiner make the following amendments to the Claims:

26. (Thrice Amended) A method for generating a database of sequences that are greater than or equal to about 100 nucleotides in length, wherein each sequence is entered into the database only one time, the method comprising the steps of :

selecting a query sequence from a redundant database, said redundant database comprising random [short] sequences of an informational biomolecule;

masking said query sequence with known repeat sequences to create a contig masked query sequence capable of masking novel repetitive elements;

comparing said contig masked query sequence with identified unique sequences;

identifying a unique portion of the query sequence that does not have a similar sequence in any of the identified unique sequences and remembering [same] said unique portion of the query sequence; and

adding the unique portion of the query sequence to a unique database [in order to reassemble the data therein via an interative learning process into an assembly with those in the known repeat/masking database], and

displaying the unique database.

28. (Original) The method of claim 26, wherein said sequence is a deoxyribonucleotide sequence.
29. (Original) The method of claim 26, wherein said sequence is a ribonucleotide sequence.
30. (Original) The method of claim 26, wherein said sequences are derived from animal DNA or RNA.
31. (Previously Withdrawn) The method of claim 30, wherein said animal is a human.
32. (Previously Withdrawn) The method of claim 30, wherein said animal is a mouse.
33. (Previously Withdrawn) The method of claim 26, wherein said sequences are derived from plant DNA or RNA.
34. (Previously Withdrawn) The method of claim 33, wherein said plant is a single-cell plant.
35. (Previously Withdrawn) The method of claim 26, wherein said sequences are derived from fungal DNA or RNA.
36. (Previously Withdrawn) The method of claim 26, wherein said sequences are derived from DNA or RNA of a microorganism or virus.

37. (Previously Withdrawn) The method of claim 26, wherein said sequences are derived from DNA or RNA of a single-cell eukaryote.
38. (Previously Withdrawn) The method of claim 26, wherein said sequences are derived from synthetic man-made DNA or RNA.
39. (Previously Withdrawn) The method of claim 26, wherein said sequences are postulated based upon amino acid sequences.
40. (Previously Withdrawn) The method of claim 26, wherein said database is encoded in a biological medium.
41. (Previously Withdrawn) The method of claim 26, wherein said database is encoded in a written medium.
42. (Original) The method of claim 26, wherein said database is encoded in an electronic medium.
43. (Original) The method of claim 42, wherein said electronic medium is a computer-readable medium.
44. (Original) The method of claim 43, wherein said computer-readable medium is addressable through an internet connection.

45. (Original) The method of claim 26, wherein said redundant database is a Public Domain Database.
46. (Original) The method of claim 45, wherein said Public Domain Database is GenBank.
47. (Previously Withdrawn) The method of claim 45, wherein said Public Domain Database is dbEST.
48. (Previously Withdrawn) The method of claim 45, wherein said Public Domain Database is TIGR.
49. (Previously Withdrawn) The method of claim 45, wherein said Public Domain Database is SwissProt.
50. (Original) The method of claim 26, wherein said comparing step further utilizes a Database Search Algorithm.
51. (Original) The method of claim 50, wherein said Database Search Algorithm is BLAST.
52. (Previously Withdrawn) The method of claim 50, wherein said Database Search Algorithm is FASTA.

53. (Previously Withdrawn) The method of claim 50, wherein said Database Search Algorithm is Smith-Waterman.
54. (Original) The method of claim 26, wherein said comparing step further utilizes a Scoring Matrix Program.
55. (Previously Withdrawn) The method of claim 54, wherein said Scoring Matrix Program is PAM.
56. (Previously Withdrawn) The method of claim 54, wherein said Scoring Matrix Program is BLOSUM.

RESPONSE TO THE DETAILED ACTION

1. Applicant appreciates the withdrawal of the rejections and/or objections not reiterated from previous office actions and will fully address the rejections and/or objections are either reiterated or newly applied.
2. Claims 26, 28-30, 42-46, 50, 51, and 54 were examined on the merits.

RESPONSE TO THE OBJECTIONS

3. Claim 26 has been objected to because of the incorrect spelling of the term “interactive,” line 12.
 - a. The objected to spelling is removed by amendment herein.

4. Claims 31-41, 47-49, 52, 53, 55, and 56 are objected to because the withdrawn claims do not have the claim text.
 - a. The missing claim text of the withdrawn claims is corrected herein.
5. The Examiner objects to the title of the invention as not being descriptive because the claimed invention is directed to the “generating a database...,” while the instant title is directed to the creating of...a sequence file.”
 - a. A new title is hereby submitted herein that Applicant believes complies with the Examiner’s suggestions.

Sequence Compliance

6. The Examiner takes the position that the application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.82 1(a)(1) and (a)(2).
 - a. The Examiner’s position is technically correct, since Fig. 3 is indeed contains nucleic acid sequences with sequence lengths that are equal to or greater than 10 nucleic acid molecules. And, Applicant is willing to submit a new computer readable form sequence listing, a paper copy for the specification, statements under 37 CFR § 1.821(f) and (g), if there is, in fact, a need to list such sequences in the listing. However, as the Examiner will likely realize, the sequence in Fig. 3 is an entirely hypothetical sequence created by the Applicant’s attorney only for sake of full description of the ability of the claimed invention to manipulate ANY nucleic acid sequence. Even if the nucleic acid sequence were that of an

actual sequence existing in nature or in some searchable sequence database, a comparison would be of no value in the examination of the present claims. To make Applicant generate the requested Sequence Listing is wasteful of the Applicant's time, his money spent to have his patent attorney generate the Sequence Listing, and worse yet, wasteful of the resources of the Patent Office, since it is merely form over substance. Applicant requests that the Examiner remove the requirement for a Sequence Listing. If the Examiner maintains this requirement over the arguments made by Applicant above, Applicant requests that the Examiner allow the submission of same prior to the case being allowed.

**RESPONSE TO THE CLAIM REJECTIONS -35 U.S.C. § 112, SECOND
PARAGRAPH**

7. The Examiner has rejected claims 26, 28-30, 42-46, 50, 51, and 54 under 35 U.S.C. 112, second paragraph.
8. Specifically, the Examiner takes the position that Claim 26 recites "random short sequences" which causes said claim to be vague and indefinite in regard to the limitation of "sequences that are greater than or equal to about 100 nucleotides in length" recited in the preamble.
 - a. Claim 26 has been amended to eliminate the size limitation of "short" from the claim language that seems to cause the vagueness to which the Examiner refers. Applicant takes the position that such a modification accurately describes the claimed invention without the "short" size

limitation. Having said that, the examiner is kindly requested to review the substantial problem encountered when searching the biological sequence databases prior to the invention, and which the invention now overcomes.

- b. For instance, the Examiner's attention is directed to the specification at p.4, line 4, et seq. where it is discussed that indeed the public databases are HIGHLY REDUNDANT, including high redundancy of sequence fragments of informational biomolecules. These redundancies render thorough systematic analysis of similarity or homology between nucleic acid sequences impractical (p. 4, L. 18 et seq.)
- c. The database created as recited in the preamble to the claim is indeed one preferably and practically consisting of sequences that are greater than or equal to about 100 nucleotides in length, since this generates a practical size that gives the researcher enough information on which to plan his experiments or with which to conduct further searching using the improved searching methods of the invention.
- d. To the contrary, the database that is being queried, that is the "redundant database" is not limited in size but may (AND almost invariably DOES) include "short" sequences (sequence fragments) that may be (AND, almost invariably ARE) randomized and redundantly iterated in the database to be searched.
- e. Thus, when read as a whole and in reference to the specification as required, the metes and bounds of said limitation are in fact clear.

9. The Examiner takes the position that Claim 26 additionally recites the limitation of “identified unique sequences,” and that there is insufficient antecedent basis for this limitation in the claim.
- a. There is no antecedent in Claim 26 for “identified unique sequences” since there is no need for one. The Examiner is kindly requested to envision what the challenge of the genomicist is in relation to using the invention on, for instance, public databases.
 - b. Since public genomic databases are rife with redundancy, repetition, incomplete sequences, chimeric sequences etc., the researcher wishing to practically and thoroughly search such a database for a unique sequence of his own selection (“identified unique sequence”) must first rid the database to be searched of these confounding reiterations. He does so by first (step one of Claim 26) selecting a query sequence from within the redundant database, second (step two of Claim 26) masking the query sequence in order to create a novel, cleaned-up query sequence (“contig masked query sequence”), and then comparing this cleaned-up query sequence with one or more unique sequences that he has identified as being of interest to his research (“identified unique sequences”).
 - c. If the Examiner believes that further clarification of this term is warranted, Applicant suggests (and hereby grants permission to do so) that the Examiner consider making an Examiner’s Amendment replacing “identified unique sequences” with “unique sequences of interest to the searcher.”

10. The Examiner takes the position that Claim 26 recites “remembering the same” and that the metes and bounds of this limitation are not clear because it is not clear what is being remembered as being the same.
- a. Applicant has amended the claim to recite (although somewhat redundantly) the “unique portion of the query sequence that does not have a similar sequence in any of the identified unique sequences” is what is being remembered.
11. Claims 26, 28-30, 42-46, 50, 51, and 54 have been rejected by the Examiner for being dependent from claim 26.
- a. Applicant maintains that he has overcome the rejections of the base claim 26 and therefore that all remaining bases for rejection of the dependent claims are likewise overcome.

RESPONSE TO THE CLAIM REJECTIONS -35 USC § 112 FIRST PARAGRAPH

12. The Examiner has rejected claims 26, 28-30, 42-46, 50, 51, and 54 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.
13. Specifically, the Examiner points to Claim 26 language reciting the limitation of “random short sequences” and that the Examiner does not find support therefore in the Specification citations previously supplied by the Applicant.
- a. The Examiner has noted that the pointed to support does disclose “sequence fragments” without specifying any sequence lengths.
 - b. Claim 26 has been amended to remove the size qualifier as noted above.

- c. Applicant maintains that the amendment made to remove the size qualifier overcomes this basis for objection and that the Examiner has already noted adequate support for same.

14. Specifically, the Examiner also points to the Claim 26 limitation of “to create a contig masked query sequence capable of masking novel repetitive elements” and takes the position that support for this limitation has not been found in the support previously cited by Applicant.

- a. The Examiner does note that the pointed to support discloses “A contig is a group of overlapping DNA segments...,” but takes the further position that such supporting Specification citations are “different from the new limitation.”
- b. Applicant apologizes in that he may not have fully cited to the complete support available for this limitation in his previous response.
- c. Having said that, the support begins as previously noted by the definition of the term “contig,” (p. 15, L. 1-8).
- d. Ample support for this limitation is further found at:
 - i. p. 18, L. 5-16 – namely discussing how one “create[s] a contig masked query sequence capable of masking novel repetitive elements;” “using rapid sequenced alignments to produce pairwise alignments, parsing the pairwise alignments and accumulating them into a buffer, reducing (masking) the pairwise alignments, and finally creating the contigs to create the new query sequence

(i.e., “creat[ing] a contig masked query sequence capable of masking novel repetitive elements”).

- ii. In addition, Claim 26 (even as as originally filed) itself makes clear to what the limitation refers in the steps that are described – select a query sequence from a redundant database, mask that query sequence to eliminate known repeat sequences, compare that masked query sequence with the unique sequences of interest to the searcher, identify unique portions of the query sequence that are lacking in any of the sequences of interest, add these unique portions into a database. Thus, it is clear from the claim language as originally filed what is meant by “creat[ing] a contig masked query sequence capable of masking novel repetitive elements.”

15. Specifically again to Claim 26, the Examiner takes the position that the limitation of “remembering same” has not been found in the instant specification.

- a. Claim 26 has been amended as discussed above to replace the “remembering same” language with a specific reference to exactly what is being remembered in the methods of the invention.
- b. Applicant takes the position that this amendment completely overcomes this basis for rejection.

16. Finally, specifically to Claim 26 and the limitation of “in order to reassemble the data therein via an interactive learning process into an assembly with those in the known repeat/masking database,” the Examiner takes the position that he has not

been able to find adequate support for this limitation in the support previously pointed to by Applicant.

- a. Claim 26 has been amended to delete the limitation.
- b. However, Applicant respectfully notes that while the precise language of the limitation in question, namely “in order to reassemble the data therein via an interactive learning process into an assembly with those in the known repeat/masking database,” is not found in the cited portions of the Specification, the Specification is replete with description of this precise limitation.
- c. p. 29, L.1-15, as originally cited does in fact summarize such a limitation in describing how the methods of the invention build over many iteration a unique file. In particular, the cited section describes in detail how initially the unique file will have none or only a few sequences resulting from the masking process, that as the processes are reiterated, the sequences in the unique file will grow in number.
- d. Even more specifically, the Examiner’s attention is drawn to the explanation of the iterative learning process for assembling the database found beginning on p. 17, L. 12 et seq. This description literally walks the reader through Fig. 1B which itself is a graphical flow diagram of the interactive (note the flow diagram has numerous decision points requiring interaction) and is reiterated (note the looping nature of the matrix depicted), ultimately as shown creating the assembly of sequences in comparison to the known repeat/masking database.


- e. Because the limitation in question can be removed from the claim without changing the intent (an interactive and iterative computational method), Applicant has amended it. This amendment now places the claim in condition for allowance.

Applicant believes that he has fully addressed each of the bases of objection and rejection raised by the Examiner and respectfully requests that the claims be forwarded to allowance.

The Commissioner is authorized to charge to McDaniel & Associates P.C. Deposit Account No. 50/1085, any fee deemed necessary to make timely the filing of this response and the continued examination.

Respectfully submitted,

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